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FROM THE 2006 NIDRR SCI MEASURES MEETING

Measurement of Sexual Functioning After Spinal Cord Injury: Preferred Instruments

Report of the National Institute on Disability and Rehabilitation Research Spinal Cord Injury Measures Meeting

Autonomic Standards Committee:

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Abstract

Background/Objective: To determine the utility of certain instruments to assess sexuality and fertility after SCI, an expert panel identified key areas to study and evaluated available instruments. These were rated according to certain predefined criteria.

Methods: The authors divided sexual issues into male and female sexual function, male reproductive function, and female reproductive function. The instruments that have been used most frequently to measure these aspects of sexual function over the past 5 years were identified by expert consensus. Finally, these instruments were subjected to a critical review.

Results: The Female Sexual Function Index (FSFI), measurement of vaginal pulse amplitude (VPA), the International Index of Erectile Function (IIEF), and the measurement of ejaculatory function and semen quality were considered appropriate measures to assess sexual responses and reproductive function after SCI. There were no measures identified to assess female reproductive function.

Conclusions: For clinical trials aiming to improve sexual function after SCI, the FSFI or the IIEF is currently preferred. Although VPA is an appropriate means to assess female sexual responses, it is only useful for laboratory studies and is too invasive for use in clinical trials. For assessment of male fertility potential, assessment of ejaculatory capacity and semen analysis are recommended.

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INTRODUCTION

People with spinal cord injuries (SCIs) have an interest in sexuality from both recreational and reproductive view points. Anderson (1) queried 681 persons with SCI about their personal priorities for recovery of function. For individuals with paraplegia, improved sexual function was the number 1 priority for recovery of function, whereas for those with tetraplegia, sexual function was second only to regaining arm and hand function.

Despite patients' documented interest (1), few clinical trials have addressed the concern of improving sexual capabilities after SCI (2,3). As part of a initiative sponsored by National Institute on Disability and Rehabilitation Research (NIDRR) and the American Spinal Injury Association (ASIA) to systematically review outcome measures after SCI, we reviewed outcome measures pertaining to sexual and reproductive capabilities and performed a detailed assessment to determine which, if any, were valid to use in an SCI population.

METHODS

Under the auspices of NIDRR and ASIA, 2 national meetings were held to present the results of a systematic evaluation of outcome measures in various areas related to SCI. Sexual function and other autonomic functions were covered in the second meeting held in 2007. For this area of sexual function, an international team of experts was chosen for their track record of research and publication. This team worked via internet and face-to-face meetings at select professional conferences to assess the state of the science with regard to measurement of outcomes in specific areas of sexual function. The team decided to evaluate sexual instruments in 4 categories—male sexual function, female sexual function, male

reproductive function, and female reproductive function—for the purpose of appropriateness for future SCI trials. The authors divided into small groups based on their individual area of expertise and performed a review of the literature identified using MEDLINE and PubMed and performing a 5-year search in addition to reviewing their own knowledge in the area.

Based on frequency of use, the group identified 5 measurement tools to assess in detail. These included the Female Sexual Function Index (FSFI) to assess female sexual function (3), vaginal photoplethysmography to assess vaginal pulse amplitude (VPA) (4), the International Index of Erectile Function (IIEF) (5) to assess male sexual function, and ejaculatory ability and semen quality to assess male reproductive capability. No measures of female reproductive capability were/could be identified. Once the literature search was completed, an expert completed the grid developed by Johnston and Graves (6) to critically assess its utility in an SCI clinical trial. The results were critically reviewed by a second committee member. Finally, the entire committee rereviewed all results.

RESULTS

Female Sexual Function Index

The FSFI is a multidimensional, self-report instrument that was initially validated in a sample of 128 able-bodied women with female sexual arousal disorder along with 131 age-matched heterosexual women ranging in age from 21 to 69 years without arousal disorder (3). The minimum score is 2 and the maximum is 36. Six domains are identified that include desire, subjective arousal, lubrication, orgasm, sexual satisfaction, and pain. The FSFI questionnaire takes about 15 minutes to complete. A total of 19 questions assess women's sexual activity over the past 4 weeks. These include 2 questions pertaining to desire, 4 regarding arousal, 4 with respect to lubrication, 4 assessing orgasm, 2 documenting sexual satisfaction, and 3 assessing pain. Based on responses to the questions, individual domain scores are obtained in addition to an overall score. These scores can be used to assess treatment responses based on individual domain scores or the overall score.

The FSFI was initially shown to have relatively high test–retest reliability ranging from 0.79 to 0.86 for the individual domains and for the total scale. Internal consistency was also documented for each of the 6 domains; Cronbach α was 0.82 or higher (3). Internal consistency was also evaluated in another study where high inter-item correlations were noted in all domains among women with female orgasmic dysfunction and control subjects (7). The only area for which internal consistency was not high was in a subset of women with hypoactive sexual desire disorder in respect to the desire category ($\alpha = 0.58$). In another group of subjects, including several samples of women with mixed sexual dysfunctions and a large sample of nondysfunctional controls, Cronbach α ranged from 0.82 to 0.97 (8).

Discriminant validity was shown in the initial sample when comparing control subjects with women with Female Sexual Arousal Disorder (FSAD), both within each domain and for the full scale score (3). Highly significant mean difference scores with $P \leq 0.001$ were shown between the FSAD and the control group for each of the domains. Discriminant validity was also documented within each domain and for the full-scale score when comparing women with female orgasmic disorder or hypoactive sexual desire disorder with those without sexual dysfunction (7). Discriminant validity was also documented using multivariate analysis of variance (MANOVA) and in a combined database of subjects with mixed sexual dysfunctions and controls [Wilks λ, $F(30, 2038) = 17.81$, $P < 0.001$, $\eta^2 = 0.17$]. Using the diagnostic groups of hypoactive sexual desire disorder, female sexual arousal disorder, female sexual orgasm disorder, sexual pain disorder, multiple sexual dysfunction, or nondysfunctional controls, significant differences were noted for the total score, desire, arousal, lubrication, orgasm, satisfaction, and pain domains (8). Receiver operating characteristic curves were also developed for the FSFI. The sensitivity and specificity curves were highest for the total score, followed closely by curves for lubrication, arousal, and orgasm. Classification and regression tree (CART) analysis was used to determine clinical cut-off scores for the FSFI total score for documenting the presence of sexual dysfunction. Using a cut-off score of 26.55 or less, 70.7% (217 cases) were correctly classified as dysfunctional and 88.2% (230 cases) were correctly classified as nondysfunctional.

Divergent validity was also documented for the FSFI. The association between the domain and full-scale scores

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of the FSFI and the Locke-Wallace Marital Adjustment test score were calculated (3,7). Overall correlations between these 2 scales were modest, thus supporting the construct validity of the FSFI.

Although the FSFI shows promise for use in clinical trials related to female sexual function, it has not yet been used widely in clinical practice. In addition, although it is currently being used in a number of research studies related to SCI, no published studies in SCI have yet used the FSFI. One potential problem in using the FSFI in SCI is the reliance on data related to sexual activities over the past month. For women with SCI, it is common for sexual activity to be less frequent than monthly. For instance, in the case of question 12, which documents difficulty in achieving orgasm, an individual might answer "no sexual activity" 1 month and then the next month they might be active but have difficulties. In this case, having extreme difficulty or being unable to reach orgasm could inappropriately appear to be an improvement in sexual response. Despite these potential problems, the content of the instrument was considered applicable to SCI, and evidence of validity and reliability has been noted in an able-bodied population; thus, the committee felt that further development of the FSFI for use in SCI is desirable.

Vaginal Photoplethysmography

Vaginal photoplethysmography entails the use of an intravaginal tampon-sized probe that contains an infrared light-emitting diode that projects light toward the vaginal wall. Some of the light is reflected back to a phototransistor, whereas the remainder is dispersed throughout the vaginal wall. As the amount of blood increases in the vaginal blood vessels, the signal returning to the photosensitive cell is thought to increase. Two types of current signals, direct and alternating, are obtained through the photocell. The direct current signal is thought to provide information regarding the change in total vaginal blood volume (VBV). The alternating current signal is thought to reflect pressure changes within the blood vessels of the vagina's vascular walls and is known as VPA. Signal cleaning must be performed to eliminate high-frequency noise and artifact. Response levels are computed for time periods of interest. For VPA, either the average or maximum value is calculated for the period of interest, or this value (in mV) is compared with baseline readings.

Because the vaginal photoplethysmograph relies on physical measurement, its use is limited to psychophysiologic research. Although this results in the added benefit of being able to eliminate confounders in sexual function research, it also results in potential bias in that subjects must be willing to be sexually active in a laboratory setting. Furthermore, there is interlaboratory variability, and it is uncertain whether findings obtained in a laboratory setting will be reflective of the subjects' usual sexual responses. Use of vaginal photoplethysmography also requires special equipment that can cost more than $10,000, thus it is a relatively expensive technique. Moreover, a dedicated space is generally required in which to do the study.

Reproducibility of VPA can be problematic. The device is inserted into the vagina, and it is not possible to assure consistency about where it is placed. Thus, baseline readings can change from session to session, and it is not possible to test study drugs or treatments within a single session. Serial studies must often be performed, and studies must be counterbalanced to account for order effects. Care must also be taken to avoid movement artifact.

A number of studies have evaluated the effects of erotic stimuli vs baseline states on VPA and VBV (9–12). The overall conclusion from these studies is that VPA is both more sensitive and more reliable in assessing vaginal responses during sexual arousal. Response specificity, sensitivity, and construct validity of VPA and VBV were measured during sexual neutral and nonsexual emotional states (11). VPA has shown response specificity to sexual stimulation. Moreover, it was superior to VBV with regard to convergent and divergent validity. Both sexually functional and dysfunctional able-bodied women have been assessed with VPA (13). Eleven women with low arousal and anorgasmia were compared with 11 nonclinical controls. No significant differences were found between the groups with regard to physiologic responses; however, the dysfunctional group reported significantly lower sexual subjective arousal. VPA has been used to assess the effects of medications on sexual arousal (14,15). In a pilot study of 6 able-bodied women with difficulty with vaginal lubrication, the effects of phentolamine vs placebo on vaginal blood flow and subjective arousal were compared (14). In another study, the effects of sildenafil vs placebo administration were compared in an experimental protocol that included viewing an erotic video and self-stimulation (15). Based on the above studies, it is concluded that VPA is currently the method of choice for measuring vaginal vasocongestion in the absence of orgasm (16).

VPA has also been used to measure vaginal blood flow in women with SCI in a number of studies (15,17–23). Its use has been coupled with detailed ASIA assessment to document the impact of specific levels and degrees of injury on vaginal vasocongestion (16–20). In SCI, it has also been used to assess the impact of medication on vaginal blood flow responses, the effects of false positive feedback and the effects of vibratory stimulation (15,21–23).

In summary, the use of vaginal photoplethysmography to measure VPA is a laboratory-based method to provide specific information about the impact of various conditions on vaginal blood flow. Although potential bias and cost are limitations, at present, it is considered the most reliable method for assessing vaginal blood flow. The frequency of its use in women with SCI is also a

strength, and the committee concluded that, at present, it is an appropriate measure to use in SCI.

International Index of Erectile Function

The IIEF is a 15-item, multidimensional questionnaire (5) that is frequently used as an endpoint in clinical trials to assess changes in erectile quality after a therapeutic intervention. The questionnaire, which has been linguistically validated in 32 languages, takes about 10 to 15 minutes to complete. Quality of male sexual function is assessed in 5 domains, with 6 items that assess erectile function, 2 items that address orgasmic function, 2 questions that assess sexual desire, 3 items that assess intercourse satisfaction, and 2 items that assess overall sexual satisfaction. The IIEF does not yield a total score, because the original questionnaire does not have numerical responses. However, for the 6 questions related to erectile dysfunction (ED), it is generally accepted that the answer categories can be ranked 0 to 5 and added for a total score of 30. It is also generally quoted in numerous studies that an erectile function domain score greater than 25 is regarded as "normal" erectile function, whereas scores of 17 to 25 are rated as mild ED, 11 to 16 as moderate ED, and 1 to 10 as severe ED.

Reliability of the IIEF was initially assessed through its use in 3 studies (n = 111 subjects with erectile dysfunction; n = 109 control subjects; and n = 37 subjects with erectile dysfunction and n = 21 controls). Internal consistency was computed separately for the 5 domains and for all items combined. Cronbach α scores were greater than 0.9 for the erectile and orgasmic function subscales and for the total score, whereas the other domains had Cronbach α greater than 0.7. Test–retest repeatability was estimated by assessing subjects in the third study twice at 4-week intervals. For erectile function ($r = 0.84$), intercourse satisfaction ($r = 0.81$), and the total scale ($r = 0.82$) repeatability was high; for the other domains, it ranged from 0.64 to 0.77.

Discriminant validity was documented by comparing responses from patients with responses from controls. Overall, the individual domain scores showed excellent discriminant validity (3). Convergent validity was shown by significant positive correlations between the individual domain scores and independent clinician ratings of the subjects' functioning. Divergent validity was documented by a lack of correlation between the domain scores and measures of marital adjustment on the Locke-Wallace Marital Adjustment test (24) or social desirability measured with the Marlowe-Crowne scale (25). Further evaluation of a sample including 1,035 men with erectile dysfunction and 116 men without erectile dysfunction was performed using CARTs to determine appropriate cut-off scores for the erectile function domain that would determine whether or not men have erectile dysfunction and its severity (26).

The IIEF has been used successfully to measure responsiveness to erection enhancement treatments and/or placebo. In the original study, each of the domains showed significant increases in scores for subjects on treatment, whereas none of the control subjects had significant increases (3). Subsequently, the IIEF has been used in more than 60 studies (27) in different ethnic populations and geographic areas, and it has served as a major endpoint in more than 50 clinical trials.

The IIEF has been used in a number of studies of men with SCI (28–31). No norms have been developed for men with SCI; doing so would be difficult because of the varying effects of different injury patterns on erectile responses. Although the IIEF has been beneficial in documenting treatment effects in SCI, it has a major shortcoming in the population: there is no acknowledgment of the issues of reflex and psychogenic erection and the lack of ejaculation in association with orgasm in men with SCI. It is also important to realize that some questions in the IIEF may be difficult to assess in men with SCI. For instance, in the ejaculatory domain, for a man to go from a score of "0" (no sexual stimulation) to a score of "1" (almost never/never ejaculate with stimulation) may indicate a problem rather than an improvement in function. Based on this concern, it may be appropriate to consider 1 as the lowest appropriate baseline score rather than 0 to be the lower limit when considering a change in sexual function.

In summary, the committee notes that the IIEF has been extensively validated in able-bodied individuals and used in studies that included men with SCI and in 5 studies specifically in men with SCI. Further use in SCI is recommended; however, it is recommended that when applied to subjects with SCI, the most common experiences after SCI be substituted for the time criterion of experience in the past 4 weeks. Moreover, the issues mentioned above should be acknowledged and addressed in future studies, and validation in a population of men with SCI would be appropriate.

Male Reproductive Function

Three factors contribute to infertility in men with SCI: erectile dysfunction, ejaculatory dysfunction, and semen abnormalities. Although the majority of men with SCI can initiate erections, the majority cannot ejaculate during sexual intercourse (32). In a survey of 199 men with SCI, only 8% reported fathering a child after injury (32). In this survey, 1 of the largest of its kind to date, a trend was found between the ability to ejaculate and the neurologic level of injury. Of respondents who had achieved ejaculation after injury, 74.7% had injuries at or above T6, 16.9% had injuries between T7 and T12, and 8.4% had lumbosacral injuries ($r^2 = 0.03$). These data are in agreement with previous laboratory-based findings with PVS showing higher ejaculatory success rates in men with higher levels of injury (33).

In addition to level of injury, the survey found several factors that were associated with successful ejaculation in men with SCI. For example, 81.3% of individuals who reported emptying their bladders by controlled voiding also reported having achieved ejaculation after injury ($r^2 = 0.07$, $\chi^2 = 17.22$, $P = 0.0085$). Likewise, 86.9% of individuals who had voluntary control of their bowels were able to successfully ejaculate ($r^2 = 0.07$, $\chi^2 = 17.93$, $P = 0.0013$), No significant relationship was found between the ability to feel touch in the anal area or the ability to voluntarily tighten the anal sphincter and having achieved ejaculation after injury (32).

For ejaculation to occur, the dorsal penile nerve must be intact, and the ejaculatory reflex in the thoracolumbar area of the spinal cord must be activated (34). The bulbocavernosus reflex (BCR) and the hip flexor response (HR) have been studied for their ability to predict ejaculation by PVS in men with SCI. The BCR and HR are indicative of intact spinal reflex arcs that are required for ejaculation. The BCR, when present, measures the integrity of the S2–S4 segment (35,36). The HR is a pathological flexion reflex commonly seen in patients with SCI (37). In these patients, firmly stroking the sole of the foot (S1) and eliciting a hip flexion response (L2–L4) presumes the integrity of the spinal cord immediately superior to the S2–S4 segments.

Studies showed that men with SCI who have a BCR and an HR were more likely to ejaculate with PVS than men without these responses (38–40). A subgroup analysis showed that the BCR and HR were more useful for predicting ejaculatory success in men whose injuries were below the cervical level. For example, in men whose injuries were between T1 and T6, ejaculation occurred in 94% of men who had a positive BCR plus a positive HR vs 0% with neither response. Similarly, in men whose injuries were between T7 and T12, ejaculation occurred in 67% of men who had both responses vs 0% with neither response. In contrast, presence of both responses was nearly as predictive as level of injury in men with cervical injuries, with an ejaculation success rate of 78% vs 50% in men with both responses vs neither response (38).

No validated questionnaires have been developed specifically to assess ejaculatory function in men with SCI. The IIEF has 2 questions that deal with ejaculation. As discussed earlier, properties of the IIEF render it inappropriate as a tool for routine assessment of ejaculatory function in men with SCI. To assess reproductive function in a man with SCI, sperm must be obtained and analyzed. If a man cannot ejaculate with sexual intercourse, he is considered anejaculatory (41). For men with SCI who are anejaculatory, the committee recommended determination of ejaculatory capability by the methods of penile vibratory stimulation (PVS) or electroejaculation (EEJ). Sperm obtained by these methods would be analyzed for quality. If sperm could not be obtained by PVS or EEJ, surgical sperm retrieval would be an option.

Penile Vibratory Stimulation

PVS is a method of inducing ejaculation in men with neurogenic anejaculation. The method of PVS involves placing a specialized vibrator on the glans penis. The vibration delivers mechanical stimulation to the penis with the goal of recruiting the ejaculatory reflex to induce ejaculation. PVS-induced ejaculation requires an intact ejaculatory reflex arc to provide transmission of afferent stimuli from the penis to the sacral, lumbar, and lower thoracic segments of the spinal cord and efferent stimuli from these segments to the ejaculatory organs, with little or no interference from the brain. It has been shown that intact dorsal penile nerves are necessary for PVS-induced ejaculation in men with SCI (42).

In 1994, Sonksen et al (43) reported on the importance of vibratory amplitude for achieving successful ejaculation by PVS of men with SCI. The study showed that an amplitude of 2.5 mm (vs lower amplitudes) and frequency of 100 Hz were optimal for inducing ejaculation in men with SCI. Although Hertz refers to oscillation frequency, amplitude refers to the distance traversed by the moving part of the vibrator, ie, how far the vibrating part is moving up and down. Based on this research, a vibrator was engineered specifically for inducing ejaculation in men with SCI. This vibrator, called the FERTI CARE Personal, continues to be the only commercially available device developed especially for this purpose (www.multicept.com).

The procedure of PVS has been well described in a number of publications (44–46). The following protocol is typically followed. Any man with SCI is eligible for PVS, although certain medical conditions are relatively contraindicated. Severe inflammation or irritation of the glans penis, which can occur in patients who wear condom catheters, is a relative contraindication because PVS may lead to further skin breakdown. Patients with untreated hypertension or cardiac disease should not be administered PVS because of a potentially dangerous increase in blood pressure. In patients with a penile prosthesis, PVS should be applied carefully to avoid pushing the glans onto the distal end of the prosthesis. Additionally, patients recently injured (ie, $<$18 months) may not respond readily to PVS because of recovery from the spinal shock phase.

For safety and efficacy, it is advisable to perform PVS after transferring the patient from his wheelchair to an examination table or hospital bed. Because of the risk of autonomic dysreflexia, the head of the bed must be able to be elevated if AD occurs. However, the PVS procedure may also be performed with the patient remaining seated in his wheelchair. The wheelchair site is recommended when transfer is problematic such as with patients who have high cervical injuries, those with severe pain or extreme obesity, or those wearing spinal cord stabilization devices. After the patient has been safely positioned, the vibrator is applied to the glans penis (dorsum or frenulum). Placement of the vibrator on the shaft of the

penis or on the perineum is less effective. Placement on the testicles is similarly less effective and could injure the testicles. The vibrator is applied for 2 to 3 minutes or until antegrade ejaculation occurs. If no ejaculation occurs, stimulation is stopped for 1 to 2 minutes, during which time the penile skin is inspected for abrasion or edema. If the penile skin is satisfactory, and there are no other contraindications, the stimulation/rest cycle is repeated. Typically, no more than 3 stimulation/rest cycles are performed within 1 PVS trial.

If a patient is unable to ejaculate with a high-amplitude vibrator, other methods may be used to facilitate ejaculation with PVS, such as application of 2 vibrators (47), use of abdominal electrical stimulation in addition to PVS (48), or oral administration of Viagra before PVS (49).

The definition of PVS failure varies among practitioners. There is a degree of uncertainty about how many trials to administer, how many minutes per trial, or what methods beyond administration of 1 vibrator should be tried before considering the patient or the trial a PVS failure. Studies have shown that patients with a BCR and an HR response are more likely to ejaculate with PVS than patients without these responses (38–40). The BCR and HR are more useful for predicting ejaculatory success in patients whose injuries are below the cervical level (38). For example, in men whose injuries were between T1 and T6, ejaculation occurred in 94% of men who had a positive BCR plus a positive HR vs 0% in men with neither response. Similarly, in men whose injuries were between T7 and T12, ejaculation occurred in 67% of men who had both responses vs 0% in those with neither response. In contrast, presence of both responses was nearly as predictive as level of injury in men with cervical injuries, with an ejaculation success rate of 78% vs 50% in men with both responses vs men with neither response.

In reality, the degree of effort and commitment to PVS will vary based on the skill and experience of the practitioner. Two consecutive failed PVS trials, spaced at least 1 week apart, typically defines the patient as a PVS failure.

The most significant risk when performing PVS is the possibility of autonomic dysreflexia (AD) in patients whose level of injury is T6 or above (50,51). AD symptoms can be well managed or prevented by oral administration of nifedipine (50,52). Patients with a level of injury T6 or above should be pretreated with nifedipine, which is typically given sublingually 15 minutes before stimulation onset. A dose of 20 mg is usually administered on the first trial of PVS and adjusted on subsequent trials based on the patient's blood pressure during PVS.

Electroejaculation

Men who cannot produce ejaculate using PVS are often referred for EEJ. EEJ is a method of retrieving semen from anejaculatory men (53,54). Unlike PVS, which may be performed at home by some patients, EEJ requires administration by a specially trained physician. To perform EEJ, the patient is placed in the lateral decubitus position. A probe is placed in the rectum. The probe contains electrodes, which are positioned toward the prostate and seminal vesicles. Electrical current is delivered through the probe, which stimulates emission of semen.

EEJ is a safe, reliable method of semen retrieval in men with SCI. The technique of EEJ has been described in numerous publications (55–58). Patients with a level of injury at T6 or above should be pretreated with nifedipine to manage possible AD.

Practitioners generally use the following protocol. Immediately before EEJ, the bladder is catheterized to completely empty it of urine and to limit sperm's contact with urine in cases of retrograde ejaculation (59). Through the urinary catheter, 10 to 20 mL of buffering medium (eg, Ham's F10 medium) may be instilled into the bladder to optimize the environment for sperm ejaculated in the retrograde direction. Rectoscopy is performed before stimulation to assure there are no preexisting lesions or colitis, which are relative contraindications for the procedure. Some clinicians leave the catheter in place during the procedure to use the balloon to block the bladder neck, preventing retrograde flow of semen, but most prefer to remove the catheter (36).

The EEJ stimulation is delivered in a wave-like pattern with voltage progressively increasing in 1- to 5-V increments until ejaculation occurs. It has been recommended, based on veterinary experience, that a low level of electrical baseline (100 mA) be maintained between voltage peaks and during ejaculation (53). However, as is discussed below, recent evidence suggests that complete cessation of electrical activity between peaks may be optimal for maximum antegrade ejaculation.

Antegrade ejaculate is released intermittently during the procedure but is usually dribbling in nature. The urethra may have to be milked. The voltages and currents that have been reported to successfully produce ejaculation range from 5 to 25 V and 100 to 600 mA, respectively. Ten to 20 stimulations are necessary for complete emptying of the system.

After the procedure, the bladder is catheterized again to empty the retrograde fraction, which may be substantial in some patients. Rectoscopy is performed after the procedure to exclude injury to the rectum.

As mentioned above, the previously recommended administration of EEJ had been to maintain delivery of electric current until ejaculation occurred (53,60). This method of current delivery, used by clinicians for many years, typically resulted in a higher proportion of sperm in retrograde vs antegrade fractions (61,62). Retrograde semen is problematic because of difficulty with retrieval and poor quality. For example, in most men with SCI, retrograde semen must be retrieved by urinary catheterization, which adds time, expense, and some risk to the

EEJ procedure. Retrograde sperm must be separated from urine by centrifugation, which requires time and proper equipment (centrifuge, pipettes, tubes, etc) and incurs more expense. Sperm from retrograde fractions generally have lower motility and viability than sperm from antegrade fractions (61–64), presumably because of the effects of urinary constituents, pH, and osmolality, as well as any toxic effects of urinary bacteria or catheter lubricant.

A study investigating sphincteric events during PVS or EEJ in men with SCI found that ejaculation was always preceded by the following pattern: initial forceful contraction of the external sphincter followed by contraction of the internal sphincter (65). The external sphincter began to relax before the internal sphincter. These data suggested that EEJ-induced ejaculation occurs through a complex neurologic pathway rather than by simple direct end organ stimulation. The sustained nature of the response to EEJ suggested that electrical stimulation should be stopped completely during EEJ to take advantage of the time during which pressure differentials between the 2 sphincters favors antegrade flow of semen and a decrease in the retrograde fraction.

This theory was tested in a "before-after" observational study by Ohl and Sonksen (39). Seven patients who had undergone an average of 5.1 EEJ procedures with the old technique (continuous baseline) were subjected to the new stimulation pattern for an average of 2.7 "new pattern" procedures. The antegrade ejaculate fraction increased from 38.9% to 67.9% (65).

Brackett et al (58) tested this new technique in a randomized study of 12 men with SCI. The EEJ trials with interrupted current delivery showed advantages over those with continuous current in several semen parameters. Interruption of the current resulted in increased antegrade semen volume (2.0 vs 0.9 mL), antegrade total sperm count (130 vs 79 million), and total antegrade motile sperm count (35 vs 25 million) (58). Many practitioners have now adopted the method of intermittently stopping electric current delivery during EEJ to increase semen volume and sperm concentration in the antegrade fraction.

Patients with complete spinal injuries can undergo EEJ without anesthesia. Those with significant sensory sparing or normal sensation will require general anesthesia for EEJ. The EEJ procedure can be painful in men with partly preserved sensation, and they may require either general anesthesia or sedation before treatment (66,67).

PVS and EEJ continue to be the most widely used methods of semen collection in men with SCI. PVS has several advantages over EEJ. Although both methods are safe, reliable, and effective (68–70), EEJ is more invasive, and the cost of purchasing PVS equipment is approximately 1/20th the cost of purchasing EEJ equipment (ie, approximately $800 vs $16,000; 2008 prices). PVS is preferred more by patients, and the semen quality obtained by PVS is usually of better quality than the semen obtained by EEJ (61,62). PVS does not require administration by a physician, and selected patients may use PVS to attempt home insemination. In contrast, an advantage of EEJ is its effectiveness in cases of PVS failure (58,71,72).

A review was performed on the ejaculatory success rates in a large series of SCI patients (73). A total of 412 men with SCI were administered 1,701 PVS procedures and 845 EEJ procedures. Patients' neurologic level of injury ranged between C2 and S4. In patients whose level of injury was T10 or higher, 88% responded to PVS, whereas in patients whose level of injury was T11 or lower, 15% responded to PVS. EEJ was performed only in PVS failures, 95% of whom ejaculated with EEJ. The 5% of men who did not ejaculate with EEJ all were patients with retained pelvic sensation who experienced pain at low voltages (1–4 V) on their first trial of EEJ and did not want to continue with further trials of EEJ under sedation or general anesthesia.

Surgical Sperm Retrieval

Surgical sperm retrieval (SSR) is a method of retrieving sperm from reproductive tissue. A variety of techniques may be used, including testicular sperm extraction, testicular sperm aspiration, microsurgical epididymal sperm aspiration, percutaneous epididymal sperm aspiration, and aspiration of sperm from the vas deferens (74–80). Unlike PVS and EEJ, SSR was not developed to treat anejaculation. Instead, SSR was originally developed to retrieve sperm from men without SCI who were azoospermic, ie, men who had no sperm in their ejaculate.

In the algorithm of sperm retrieval methods in men with SCI, SSR should be performed only if PVS and EEJ fail or are not possible. Relative to PVS and EEJ, SSR is an expensive and invasive method that results in a lower yield of total motile sperm. The low yield of sperm from SSR commits the couple to the most invasive and expensive of the assisted conception methods, namely intracytoplasmic sperm injection. The higher sperm yields possible with PVS and EEJ widen the options for assisted conception, potentially significantly reducing the cost and invasiveness to the couple.

Semen Analysis

To become a biological father, sperm from the male must be combined with eggs from the female partner. Natural conception occurs when sperm deposited during sexual intercourse travels through the female reproductive tract to fertilize the egg, resulting in an embryo that must then implant itself in the uterus to create a pregnancy. For 2 reasons, natural conception is not possible for most men with SCI. First, more than 90% of men with SCI cannot ejaculate during intercourse, and therefore, although they may have intercourse, they cannot deposit sperm appropriately in the female reproductive tract. Second, semen quality is abnormal in the majority of men with

SCI. Most men with SCI have semen with normal sperm concentration but abnormally low sperm motility. Because this semen profile is uncommon in the general population, numerous studies have been performed to determine the underlying cause(s) (69,72,81–86).

Similar to men with other illnesses, there is a broad range of observed semen quality in men with SCI, most of who exhibit the semen profile described above. This range varies from the occasional near normal semen specimen to the occasional azoospermic (no sperm in the semen) specimen. Semen analysis is a method of examining the ejaculate for sperm parameters, such as volume, count, motility, and morphology, which are important for the assessment of male fertility.

The classic definition of male fertility is the production of a pregnancy through sexual intercourse, and there are generally accepted standards of normal semen quality. The most universally accepted standards are those found in the World Health Organization Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction (87). These standards are based on a worldwide consensus arrived at in much the same manner as the worldwide consensus that produced the International Standards for Neurological Classification of Spinal Cord Injury, ie, through a large panel of andrology experts who, based on their clinical experience with populations of fertile and infertile men and based on their review of the vast clinical and basic science literature on human semen quality, developed reference values for semen quality.

The term "reference values" rather than "normal values" is used for semen quality because the minimum absolute values necessary for fertility have not been established. In general, studies have shown that pregnancy rates are positively correlated with numbers of total motile sperm inseminated (54,88,89).

CONCLUSIONS

Most instruments used in the spinal cord–injured population have been extensively used and validated in able-bodied populations. For the performance of clinical trials after SCI, only 2 measurements seemed appropriate to measure sexual capacity: the FSFI for women and the IIEF for men. Each has some shortcomings, and although used in populations inclusive of SCI, have not been specifically validated for SCI. Fertility measures in men who are anejaculatory after SCI include the determination of ejaculatory capacity by the use of PVS, EEJ, or surgical aspiration to obtain sperm, which is evaluated by the standard semen analysis used in any study population.

Future research should include the validation of instruments in the broad population of persons with SCI in addition to determining the validity of instruments in specific subpopulations of persons with SCI. Furthermore, validated instruments should be developed as a complement to the recently described International Standards for the Autonomic Classification of SCI (90), so that clinicians and clinical researchers will able to accurately describe the impact of any new therapies on sexuality after SCI.

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